HARVARD MEDICAL ALUMNI BULLETIN

ARTHRITIC STUDIES AT HARVARD

January, 1936

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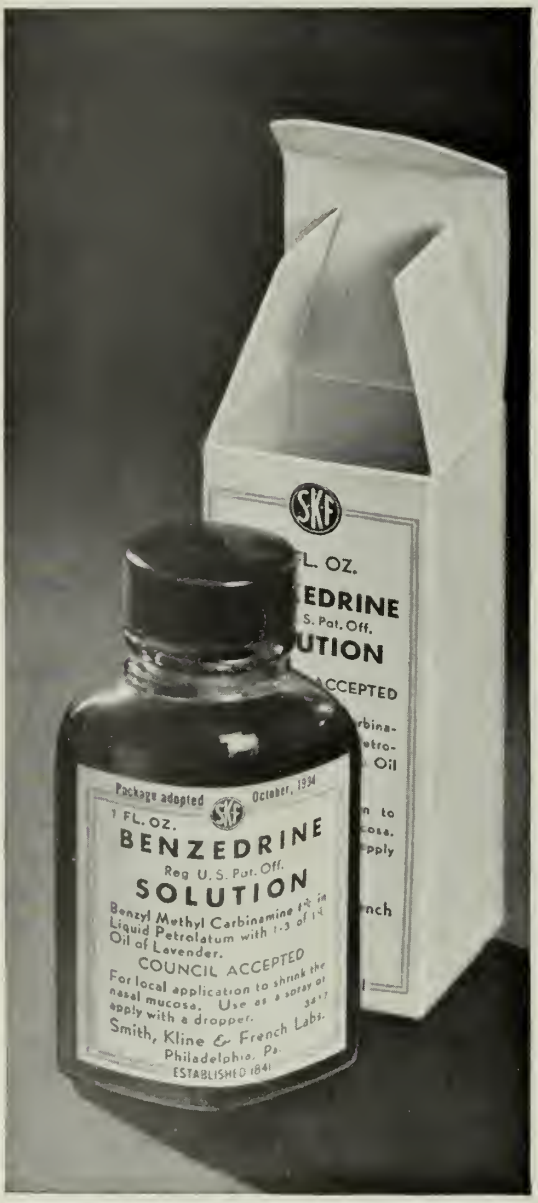

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ROBERT W. LOVETT, M.D. '85

Courtesy of Journal of Bone and Joint Surgery

Volume 10 *January, 1936* *Number 2*

Arthritic Studies at Harvard

I. At The Massachusetts General Hospital

By Charles L. Short, M.D. '28.

IN 1925, shortly after the death of Dr. Robert W. Lovett, the raising of a fund to be devoted to the study of crippling disease was started under the active leadership of Dr. Frank R. Ober. In the last five years, the investigation of arthritis, carried on jointly at the Massachusetts General Hospital and the Harvard Medical School, has been supported in great measure by this fund. It is unnecessary to recall to Harvard alumni Dr. Lovett's achievements. I need mention only his work as Professor of Orthopedic Surgery, as a teacher of army officers during the War, as the organizer of the "Vermont Plan" for the after-cure of poliomyelitis victims and as chief surgeon at the Children's Hospital and the New England Peabody Home for Crippled Children.

The aim of the Lovett Fund is to carry on his work and give an opportunity in this country for the study of conditions resulting in crippling deformities. At present, this study is concentrated on arthritis, which admittedly stands out among possible choices in incidence, in the production of disability, in economic importance and in unexplored territory for research. Since 1930, the work has been in charge of Dr. Walter Bauer, Assistant Professor of Medicine, aided by Drs. Granville A. Bennett and Frederic W. Rhinelander, II, of the Department of Pathology, and Drs. Alexander Marble, A. O. Ludwig, Marian Ropes, Charles F. Warren, H. C. Coggeshall, and the writer —all past or present members of the Department of Medicine.

It was felt at the outset that the work could best be carried out by combining fundamental investigation with careful, detailed studies of patients with the disease. In organizing the brief outline presented here, I have separated the material into two groups, although their interdependence must be stressed.

A. *Fundamental Studies.* An attempt has been made to define as completely as possible the nature and origin of normal synovial fluid. A neighboring slaughterhouse has been utilized in this work, since amounts of synovial fluid, large enough for detailed chemical analysis, along with arterial blood, can thus be obtained at or shortly after the death of cattle. Preliminary observations tend to show that synovial fluid is a simple diffusate, with the addition of mucin. At the same time, the cellular composition of normal synovial fluid has been determined in this species. Other studies pertaining to synovial fluid cytology have included the possible causes of observed cellular variations; the determination of the exact cytology of normal human synovial fluid; and the correlation of cellular variations with the histological appearance of the synovial membrane obtained immediately post-mortem from patients without joint disease, dying with or without infection. Such information is necessary before we can properly interpret the cytological changes occurring in joint effusions.

A series of investigations has been done or is in process to determine the factors influencing the drainage of normal joints both through the lymphatic and vascular systems. True solutions, proteins and other colloids, and particulate matter have all been utilized, with attention directed toward the influence of inflammation, syno-

vial fluid removal and exercise. Such information should enable us to devise methods which would allow us to determine why a joint effusion occurs, why it persists, and how it should be treated.

Mucin, the missing link in the complete understanding of normal synovial fluid, has been isolated in dry form by Dr. Ropes so that it will dissolve in normal serum and Ringer's solution. Dr. Ropes is now engaged in the laborious work of defining this substance chemically, determining its molecular size, its osmotic pressure, its solubilities and what rôle it plays in the fluid exchange of normal and pathological joints. This work should be of much greater physiological significance than that pertaining to joints alone.

Studies have been made of surgically created articular cartilage defects in mature and growing dogs as well as spontaneous degenerative cartilage lesions probably due to trauma occurring in cattle. These studies reveal that the ability of articular cartilage to repair itself is at best feeble. This inability of articular cartilage to repair seems to bear a direct relationship to hypertrophic (degenerative) arthritis and has been supplemented by examination of the knee joints of patients from the first to the ninth decades without obvious joint disease. This last reveals that with increasing age, one observes increasing degenerative joint changes indistinguishable from so-called hypertrophic arthritis. The results of these studies and the changes observed in patellar displacement, unusual use, or trauma make us question the use of the word "arthritis" in this type of joint disease.

Finally, the changes in the synovial membrane produced by intra-articular injection of supposedly innocuous solutions, the formation and development of the human knee joint, and the pathology of all types of joint disease are being studied.

B. *Clinical Studies.* Those of you who are engaged either in private or hospital practice are well aware of the only too abundant arthritic clinical material presenting itself. We decided therefore not to open an "arthritic clinic" in the out-patient department such as had been in existence at times in the past where we would soon be swamped with patients with all types of joint disease. A fresh start was made by organizing a complete study according to a systematic plan of each patient entering the medical wards with definite rheumatoid arthritis. This group now numbers well over three hundred. A careful history and examination is made of each one along with detailed roentgenological and laboratory studies, and the data are entered on a sheet lending itself to statistical analysis. This analysis is now in process with the aid of Professor Wilson of the School of Public Health, and we hope in this way to confirm or disprove many of the statements found in the literature.

On discharge from the hospital, the patients are followed at regular intervals in the out-patient department and the clinical course of this disease, so prone to remissions and relapses, can thus be observed and defined. Once a week, rounds are made by the group on all patients with joint disease in the wards, and opinions and suggestions written into the records. Biopsies of subcutaneous nodules, muscles, and tissue removed at operation are obtained from time to time from these same patients. Complete autopsies are made whenever possible. In this way a large teaching collection is being built up from carefully studied cases.

In addition, nearly routine aspiration is done in all types of joint disease of joints containing appreciable effusion, with cytological, chemical, bacteriological and immunological study of the fluid obtained. As these data accumulate, synovial fluid examination may turn out to be useful in a diagnostic and prognostic sense, just as we now employ the spinal fluid.

On a small number of patients with both types of the disease, studies of calcium, phosphorus and creatin metabolism have been carried out in the metabolic ward.

Tests for activity, including the sedimentation rate, Schilling counts, Vernes resorcinol test and streptococcus agglutinations have been done and correlated with the clinical course. To date, the sedimentation rate has been found the most reliable and accurate.

With the coöperation of Dr. T. Duckett Jones, Research Director of the House of the Good Samaritan, all of the important streptococcal immunological tests have been performed at repeated intervals on a large group of rheumatoid arthritics over a year's period. This study should enable us to state more definitely what rôle the streptococcus plays in the etiology of rheumatoid arthritis.

Since the work is carried on in a general hospital, we find many cases with joint signs and symptoms labeled arthritis when some other etiology is present. This has brought out the importance and frequent difficulties in differential diagnosis. We have found conditions ranging from pulmonary osteoarthropathy to multiple osteomyelitis masquerading under the diagnosis of arthritis. It has likewise taught us that recurrent gout is a relatively common disease which all too often goes unrecognized. Gonorrheal arthritis, of course, has frequently presented itself. Detailed studies, therefore, are being made of the clinical course and varied findings in a series of one hundred odd cases. A study has been made, in addition, as to the value of the gonococcal complement fixation reaction as a diagnostic aid in patients with all types of joint disease.

We have adopted no set line of therapy, but have given the patients the usual general and dietary treatment along with removal of obvious foci when indicated. We have enjoyed the full coöperation of the Orthopedic Service in instituting preventive or corrective measures. We have tried to avoid so-called specific treatment in order better to evaluate the course of the disease as well as to accumulate some much needed control data. Two of the more recently proposed methods of therapy, fever induced by general diathermy, and the use of "autogenous vaccines," have been carefully and critically tried with negative results.

Finally, the group has contributed to the review of American and English literature on arthritis, published annually by the American Association for the Study and Control of Rheumatic Diseases.

It is hoped that it will be possible for this work to continue uninterrupted for an indefinite period of time. In this way we should eventually be able to obtain a more complete knowledge of the anatomy and physiology of normal joints and a better understanding of all joint disease. A continuous study of this sort is made possible only by the establishment of endowments such as the Robert W. Lovett Memorial Foundation. Research into chronic disease will require more such endowments and even larger ones.

II. At The Thorndike Laboratory

By Chester S. Keefer, M.D.

DURING the past four years my associates and I, at the Thorndike Memorial Laboratory, Boston City Hospital, have been interested in the study of various types of arthritis. So far, the studies have been carried out in accordance with the following plan.

(1) An anatomical study of the joints of individuals with and without various types of arthritis.

(2) The characteristics of the synovial fluid in various types of arthritis.

(3) A study of the various serological reactions in the blood and synovial fluid of

patients with various types of joint disease; their relation to the etiology and course of the disease.

(4) An investigation of the various factors influencing the pathogenesis and clinical course of various chronic disorders of the joints.

The anatomical studies are made possible through the collaboration of Dr. Frederic Parker, Jr., the Director of the Mallory Institute of Pathology of the Boston City Hospital. Gross and microscopic studies of joints from individuals of various ages have been examined to determine the variations in structure with advancing age. In addition, the different factors of importance in causing degenerative lesions are being investigated and analyzed. This type of study is necessary in order to establish variations from the normal structure of the joints at various age periods, and to assess the influence of different factors responsible for bringing degenerative changes into being.

There is clear evidence that degenerative changes in the various movable joints increase as age advances, and that these alterations in structure are identical with the anatomical lesions described previously as being characteristic of hypertrophic or osteo arthritis. The pathogenesis of such lesions can be attributed to constant wear and tear of movable parts, and to such factors as excessive weight bearing and static defects. Previous gross injuries to the joint surfaces serve as accelerating factors. There is no supporting evidence that these degenerative lesions result from vascular disease, infections, or disorders of calcium metabolism. Moreover, it is plain that the sequence of events in the development of degenerative arthritis is quite distinct from that in rheumatoid arthritis.

Aside from the anatomical changes which appear with increasing age, the alteration in the structure of the joints during various infections are being studied and compared with normal joints, and those showing degenerative changes. In this way, it is possible to obtain information regarding the mode of infection, and the type of reaction in the tissues of such joints.

The purpose of the studies on the synovial fluid in various types of arthritis is to determine the value of synovial fluid examinations as an aid in the diagnosis, prognosis, and treatment of diseases of the joints. Cytological, chemical, bacteriological, and serological examinations are being made, and information regarding etiology, the character of the injury to the tissues, and the prognosis of various types of arthritis is being obtained.

One part of the work that has commanded attention is the mechanism of recovery in gonococcal arthritis. Methods for the study of the various antibodies against the gonococcus have been developed, and are being employed in the study of the blood and synovial fluid. These findings, together with information that is being accumulated from the character of the tissue reaction, as reflected by the synovial fluid, is providing information of significance in prognosis and treatment.

For many years, it has been known that streptococcal infections are frequently followed by acute arthritis of a non-suppurative character. Recently, the presence of hemolytic streptococcal agglutinins in the circulating blood of patients with rheumatoid arthritis has been demonstrated by a number of observers. The precise significance of this fact cannot be interpreted with certainty at the moment. In order to shed more light on this problem, the various serological reactions following proved hemolytic streptococcal infections are being examined. In this way, more information may be obtained and a clearer understanding of the findings in rheumatoid arthritis may be discovered.

The purpose of the studies that have been undertaken is to add information regarding the pathogenesis, clinical course, and treatment of various types of arthritis, on a rational and logical basis. Financial assistance has been received for several years from the Proctor Fund, and the Milton Fund and Clark Bequest.

III. At The Robert B. Brigham Hospital

By Loring T. Swaim, M.D. '09

ACCORDING to the Massachusetts Statistics, published by Bigelow, chronic arthritis is our most common disease. During the last fifteen years the interest in chronic arthritis has increased enormously. More and more work is being done in an attempt to find its cause and the best methods of treatment.

In 1914 Mr. Robert Breck Brigham and his sister bequeathed a hospital which should take care of the chronically ill of greater Boston. Because of the special interest taken in arthritis, the hospital has gradually become a center for special study of the more difficult cases. The work has had two primary objectives; first, the treatment and care of the patient and second, research. One of the unique features of the arrangements is that any case can be kept under observation as long as necessary, not only for the patient, but for study.

The hospital is a complete unit except for a bacteriological laboratory. Such work has to be done outside the hospital. It has excellent hydro, physio, and occupational therapy departments. The chemical laboratory is completely equipped to do any kind of chemical and clinical research. Besides all the usual medical departments, there is a dental department as all chronic patients need constant supervision of their teeth. Much remains to be learned about tooth infections in arthritis.

One of the important things in the study of arthritis is the correlation of facts. There are certain hereditary tendencies in the atrophic type of arthritis which are essential to know. The age and the sex frequency are also important, as well as the accumulation of the knowledge of diseases which are associated with arthritis.

Studies have been made by serial X-rays in order to acquire knowledge of the changes which are occurring in joints from year to year. This has been most instructive and interesting and has thrown much light on the apparent loss in function as the disease improves.

Much time has been spent in the laboratory studying the vital capacity, the sedimentation rate, the basal metabolism rate, the kidney function, gastric analysis, sugar tolerance, variations in calcium and phosphorus determinations, and the study of sweat. Blood studies have revealed that there is almost always a secondary anemia present in the atrophic cases. The sedimentation rates are high in the active disease and about 60 per cent of the cases show a low sugar tolerance, low basal metabolism and a low blood pressure. The vital capacities, calcium and phosphorus determinations, kidney function tests, and the gastric analyses have not shown any particular variations which were of great significance. The study of sweat has shown the tendency to acid sweat which decreases as the patient improves or after a series of steam baths. The exact significance of this is not yet known.

Another research has been the study of different features of treatment such as the high and low carbohydrate diet, and the effect of thyroid medication in cases of low basal metabolisms. It has been surprising to find that few cases respond in their basal metabolic rate to the administration of thyroid. An attempt has been made to estimate the effect of treatment by the change in the sedimentation rate, but this has been rather baffling so far.

The beneficial effects of general massage and heat, both moist and dry, has been definitely proved, particularly with the use of steam baths, with frequent sweating. Systematic exercises and judicious use of hydrotherapy has been extremely beneficial in increasing the resistance and health.

Another point of the hospital program has been to watch the effects of removal of foci, in the throat, sinuses and teeth. Much study has been done on the gastro-intestinal tract with X-rays, diet, and irrigations.

Much time has also been spent in perfecting methods of using plaster for the prevention of deformities, with the result that it has become a well known fact that local, as well as general, rest is essential for the recovery of joints and that joints improve much more rapidly with support and protection by plaster splints and simple bits of orthopedic apparatus than they do without, and that most deformities, if treated early, can be prevented. It has been clearly demonstrated that the overuse of joints is extremely bad for them, particularly during the active stages.

Much work has also been done on the surgical reconstruction of deformed joints with the development of a very successful operation called "posterior capsuloplasty." Information has been correlated as to when to operate and what operations are successful.

One of the unique features of the work has been the follow-up system in the Home Service Department, where we have our own district nurse. Patients are brought to the hospital as required, and a yearly check-up has been organized which will give us valuable data as to the course of the disease. An attempt is made to get a complete picture of the disease as far as possible. The work has been along clinical research lines to determine the best methods of treatment and those which will stand the test of time.

IV. At The Peter Bent Brigham Hospital

By Robert T. Monroe, M.D.

THE arthritic clinic in the Peter Bent Brigham Hospital was established fourteen years ago by Dr. Francis Cooley Hall for the purpose of determining what could be done by the general practitioner for the individual with chronic joint disease. Reliance was placed chiefly on careful history taking, social investigation and physical examination. Treatment was directed toward improving whatever appeared to be wrong with the patient, regardless of its bearing on his arthralgias. Much ingenuity was used to devise simple measures to correct or alleviate mechanical abnormalities. Every effort was made to keep the patient ambulatory and at his usual work. A follow-up system was employed to check results and observe what the life history of arthritis might be.

For eight years Dr. Hall worked alone, perfecting his method of clinical investigation. Then the writer came, later taking charge. Other workers were added until now the clinic is well staffed. Dr. Charles F. Walcott has assisted for two years, and there is usually a volunteer graduate student. Dr. J. C. Noll of Ohio served in 1934-35, and Dr. M. C. Loizeaux of Wellesley in the current year. Miss Katherine Weitzel has rendered intelligent service as dietitian for four years. Miss Grace Revere has acted loyally as a volunteer worker, particularly along physiotherapeutic lines. The Social Service Department, through Miss Margery Crothers, has been invaluable in solving our many economic and personal problems. Funds raised from sources known only to Miss Crothers and Miss Revere have recently made it possible to add a half-time laboratory technician. Dr. William T. Green and Dr. Meier C. Karp are now associated as orthopedic surgeons, and the

clinic has become a Medical-Orthopedic Clinic.

There are 568 patients on our rolls, of whom approximately 75 per cent keep in touch with us. Our clinic day averages twenty patients. These resources have made it possible to use the clinic for teaching two groups of post-graduate students annually. For the last three years a voluntary course in arthritis for undergraduate students has met with good response.

Investigative work has by choice been confined to clinical subjects. Articles have been published dealing with gastro-intestinal distress associated with arthritis, with hypothyroidism and myxedema in arthritis, and with the incidence of cardio-vascular disease in arthritis.

PUBLIC LECTURES

The Faculty of Medicine of Harvard University offers a course of free public lectures on medical subjects, to be given at the Medical School, Building D, Longwood Avenue, Boston, on Sunday afternoons, beginning January 5, at four o'clock.

Jan. 5—Dr. D. F. Jones, '96. Cancer.

Jan. 12—Dr. J. H. Blaisdell, '11. Cosmetics—Safe and Dangerous.

Jan. 19—Dr. H. C. Stuart. The Prevention of Infectious Diseases.

Jan. 26—Dr. W. L. Aycock. Infantile Paralysis.

Feb. 2—Dr. L. M. S. Miner. The Prevention and Treatment of Physical Diseases of the Mouth.

Feb. 9—Dr. F. C. Hall, '17. Gout and Allied Conditions.

Feb. 16—Dr. W. H. Robey, '95. The Prospect of Keeping a Good Heart.

Feb. 23—Dr. Henry Jackson, Jr., '19. The Rôle of the White Blood Cells in Health and Disease.

Mar. 1—Dr. Reginald Fitz, '09, Dr. E. C. Cutler, '13. Appendicitis.

Mar. 8—Dr. W. B. Castle, '21. Vitamins.

Mar. 15—Dr. Hallowell Davis, '22. Hearing and its Conservation.

Mar. 22—Dr. H. L. Lombard. Chronic Disease at the Cross Roads.

REID HUNT TO RESIGN

Reid Hunt, M.D., Professor of Pharmacology, has presented his resignation to take effect next September. He has filled his post at Harvard since 1913. Before that time he taught at the College of Physicians and Surgeons, New York City, and at the Johns Hopkins University, and from 1904 to 1913 was chief of the division of pharmacology in the U. S. Public Health and Marine Hospital Services.

CURRENT ACTIVITIES AT THE HARVARD MEDICAL SCHOOL, COURSES FOR GRADUATES

Feb. 6-Mar. 5. Operative Urology. Given by Dr. J. Dellinger Barney at the M. G. H.

Feb. 10-Mar. 21. Anatomy of Nose and Throat. Given by Professor Mosher at the H. M. S.

Feb. 17-Mar. 28. Medical and Surgical Diagnosis and Treatment. Given by Staff of Peter Bent Brigham Hospital.

March 23-May 2. General Course in Orthopedic Surgery. Given by Professor Ober at the Children's Hospital, M. G. H. and H. M. S.

April. "All-Day" Course in Otology. Given by Dr. Harry P. Cahill and assistants at the H. M. S. and Massachusetts Eye and Ear Infirmary.

May. "All-Day" Course in Ophthalmology. Given by Staff of Massachusetts Eye and Ear Infirmary.

Offered Monthly. Courses in Pediatrics, Roentgenology, Anaesthesia, Obstetrics, Dermatology and Syphilology, and Ophthalmology.

DR. BOWMAN GOES TO NEW YORK

Dr. Karl M. Bowman has been appointed director of the psychiatric division of Bellevue Hospital, New York City. Dr. Bowman is now chief medical officer of the Boston Psychopathic Hospital and professor of psychiatry at the Harvard Medical School.

HEADS CHEMISTRY DEPARTMENT

Cyrus H. Fiske, '14, has been appointed Professor of Biological Chemistry at the Harvard Medical School. He has already served as associate professor in that department.

DR. FITZ RESIGNS

Reginald Fitz, '09, Associate Professor of Medicine and Physician to Students at the Harvard Medical School, has been appointed director of the Evans Memorial Hospital and Professor of Medicine at the Boston University School of Medicine. At the end of the current academic year he will retire from his offices at the Harvard Medical School and from the staff of the Peter Bent Brigham Hospital.

IN HONOR OF DR. AYER

A dinner was given at the Tavern Club, Boston, on November 26 for James Bourne Ayer, '07. Dr. Ayer is James Jackson Putnam professor of neurology and has completed his first twenty-five years of teaching in the Harvard Medical School.

DR. ADLER DIES

Herman M. Adler, psychiatrist, and a member of the Harvard survey of crime and law, died at Phillips House, Massachusetts General Hospital on December 7, 1935. Dr. Adler was assistant professor of psychiatry at the Harvard Medical School from 1912 to 1917. At the time of his death he was Professor of Psychiatry at the University of California. Death was due to hypernephroma.

BOOK REVIEW

Tuberculosis of the Lymphatic System, by Richard H. Miller, M.D. '10, F.A.C.S. Price, $4. Pages, 428. Macmillan.

This book of Dr. Miller's fills a very real place in the literature of tuberculosis. I know of no other volume devoted to this important subject. An introduction to the general subject is excellently written and is of great interest.

The arrangement of chapters into clearly indicated sections with the principal references at the end of each chapter makes its reading easier. The trend of the book is sane and sound, emphasizing a part of treatment which is usually much neglected by the average surgeon, namely, the importance of the general, hygienic and constitutional treatment of the patient as well as the surgical treatment of his tuberculous glands.

Dr. Miller has handled the difficult subject of immunity and allergy very well although of course there are bound to be differences of opinion in regard to these points. There are many who will not altogether agree with what he says concerning immunity in tuberculosis but on the whole his position is a sound one.

The book is of a size and type which will make it extremely beneficial to any physician desiring to know something of tuberculosis of the lymphatic system.

John B. Hawes, 2d, M.D. '03

MEDICAL SOCIETY OF NEW YORK

The Harvard Medical Society of New York has reëlected Grant P. Pennoyer, '19, president; James F. Faulkner, '13, treasurer; and Carl H. Fornell, '14, secretary.

OLDEST GRADUATE DIES

William Lewis Macdonald, '65, died at Malden, Mass., September 24, 1935. He was the oldest graduate of the School, and died at the age of 101. He entered the practice of dentistry rather than medicine, and retired in 1910.